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June 8, 2006

Mr. Stephen Johnson, Administrator  
U.S. Environmental Protection Agency  
Ariel Rios Building, 1101-A  
1200 Pennsylvania Ave., N.W.  
Washington, DC 20460

Subject: Public comments on the HPV test plan for **3-Cyclohexene-1-carboxylic acid, 3-cyclohexen-1-ylmethyl ester**

Dear Administrator Johnson:

The following comments on Dow's test plan for the chemical **3-Cyclohexene-1-carboxylic acid, 3-cyclohexen-1-ylmethyl ester**, are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

The Dow Chemical Company submitted its test plan on December 29, 2005 for the chemical **3-Cyclohexene-1-carboxylic acid, 3-cyclohexen-1-ylmethyl ester** (CAS No. 2611-00-9), also known by its trade name, Diene 221. This chemical is a closed system intermediate produced by the reaction of two moles of tetrahydrobenzaldehyde (THBA), another HPV chemical sponsored by Dow, and then reacted with peracetic acid to produce a final product. It would be useful to know the identity of the final product and how it is used in commerce; Dow does not mention this in the test plan. Nevertheless, Dow has drawn upon existing data for the precursor chemical, THBA, to fill the endpoints for ecotoxicity and health effects. Because Diene 221 is a closed system intermediate, repeated dose and reproductive toxicity endpoints are not required in the HPV program. For the remaining endpoints, **physicochemical** properties and environmental fate, Dow has submitted data generated by *in silico* estimation models and appropriately concludes that no additional animal testing is required.

Both Diene 221 and THBA are expected to metabolize to the same degradation product, tetrahydrobenzoic acid, and therefore, THBA is an appropriate surrogate for Diene 221. Dow has indicated that **physical/chemical** measurements will be repeated and we support the use of experimental data on Diene 221 to provide additional evidence for its similarity to the surrogate chemical, THBA. In addition, Dow presents modeled data for the hydrolysis of Diene 221. We recommend that an OECD 111 study be conducted at a pH appropriate to the stomach conditions of mammals. We believe this will demonstrate that

Diene 22 1 is, in fact, rapidly hydrolyzed and any toxic effects in mammals would be due to the degradation product(s), not the parent chemical.

Existing data for Diene 22 1, as well as data from the surrogate chemical, were used in a read-across approach to fill almost all SIDS endpoints for **physicochemical** properties, environmental fate, and human and ecological toxicity. We support Dow's hazard and exposure analysis for this chemical and concur that no additional animal studies are required under the HPV program. We also note that the EPA did not recommend additional testing for reproductive/developmental toxicity for THBA, due to the corrosive nature of the chemical. Thank you for your attention to these comments. I may be reached at 202-686-2210, ext. 327, or via e-mail at *meven@pcrm.org*.

Sincerely,

**Megha Even, M.S.**  
Research Analyst

Chad B. Sandusky, Ph.D.  
Director of Toxicology and Research